



APR 11 2003

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

Via Federal Express

WARNING LETTER

Mr. L. Joe Austin
Chief Executive officer
Huntsville Hospital
Institutional Review Board
101 Sivley Road
Huntsville, Alabama 35801

Dear Mr. Austin:

The purpose of this Warning letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection of your Institutional Review Board (IRB), and to request your prompt reply. During the period of December 9 through December 19, 2002, Ms. Pamela M. Thomas, an investigator from the Food and Drug Administration (FDA), New Orleans District Office, inspected the institutional review board (IRB) at your facility. The purpose of this inspection was to determine whether your IRB's activities and procedures relating to investigational studies of FDA-regulated products complied with applicable FDA regulations.

We have completed our review of the report submitted by the New Orleans District Office which described and documented deviations from the requirements of Title 21, Code of Federal Regulations (21 CFR), Part 56 - Institutional Review Boards, Part 50 - Protection of Human Subjects, and Part 812-Investigational Device Exemptions. These deviations were listed on the Form FDA 483, "Inspectional Observations," that was presented to and discussed with you: [REDACTED] and [REDACTED], at the conclusion of the inspection.

The description of deviations that follows is not intended to be an all-inclusive list of the IRB's deficiencies.

Failure to conduct adequate continuing review of the research (21 CFR 56.109(f)).

When conducting continuing review of studies, the IRB failed to obtain all pertinent information to adequately assess whether studies should be amended, terminated, or allowed to continue as originally approved. For example:

- The November 2002 "Huntsville Institutional Review Committee Annual Continuing Review of Investigational Study" report submitted by [REDACTED] for the [REDACTED] study, indicates that one of the subjects enrolled in the study died. On 11/19/02 the IRB approved continuance of this study for another year without determining whether the subject's death was study related.
- At the time the IRB was conducting continuing review of the [REDACTED] study on 08/13/02, there was a local serious adverse event (SAE) report pending from the SAE Subcommittee. The IRB approved continuance of this study for another year without knowing the recommendation of the SAE Subcommittee.

Failure to prepare and follow written standard operating procedures (SOPs) governing the functions and operations of the IRB (21 CFR 56.108(b), 21 CFR 56.115(a)(6), and 21 CFR 812.66)).

The IRB's SOPs, entitled "Policy of the Health Care Authority of the City of Huntsville," lacked the following:

- procedures for ensuring prompt reporting to the IRB of any unanticipated problems involving risks to human subjects or others;
- procedures for ensuring that the IRB provides adequate continuing review of approved studies; and
- procedures for determining whether an investigation involves a significant or non-significant risk device.

Furthermore, the IRB's SOPs state that "each study shall be reviewed annually unless otherwise determined by the Institutional Review Committee;" and that "communication from the IRB Chairman to the investigator will include the next review period." However, approval letters sent to the investigators do not always indicate the frequency of periodic review of the study.

Failure to require adequate informed consent (21 CFR 50.25(a)(7)) and (21 CFR 56.109(b)).

The IRB failed to require that information given to subjects as part of the informed consent for the [REDACTED] study include information on whom to contact regarding medical questions and subjects' rights.

Failure to ensure that research is reviewed free from conflict of interest (21 CFR 56.107(e)).

A review of your 11/19/02 meeting minutes revealed that one IRB member failed to abstain from voting on the [REDACTED] even though she is listed as the principal investigator of that study in the meeting minutes. FDA regulations state that no IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflict of interest, except to provide information requested by the IRB.

Failure to maintain meeting minutes in sufficient detail (21 CFR 56.115(a)(2)).

FDA regulations require that an IRB prepare and maintain adequate documentation of IRB activities, including meeting minutes, in sufficient detail.

Meeting minutes reviewed failed to include specifics regarding the IRB's determination of whether studies involved significant or non-significant risk devices; the continuing review and outcome for each study; and the frequency of periodic review for each study.

Within fifteen (15) working days of receipt of this letter, please inform FDA of the corrective actions taken to remedy the deficiencies noted above. If additions and modifications to the SOPs cannot be completed in time to be included with this response, please provide a time table for when we can expect to receive them. Failure to respond to this letter and to take prompt action to correct these violations may result in regulatory action without further notice, including disqualification of the IRB.

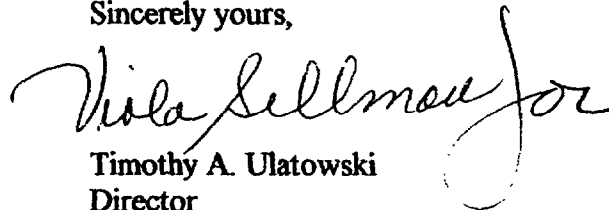
Please send all information requested to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-312), 2094 Gaither Road, Rockville, Maryland 20850. Attention: Pamela M. Reynolds.

A copy of this Warning Letter has been sent to the FDA's New Orleans District Office, 6600 Plaza Drive, Suite 400, New Orleans, Louisiana 70127. We request that a copy of your response also be sent to the New Orleans District Office.

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Please direct all questions concerning this matter to Ms. Pamela Reynolds at (301) 594-4723, ext. 155.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Timothy A. Ulatowski".

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health

cc: Kristine Borrow, Ph.D.
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